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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

The association of body composition parameters with nonalcoholic hepatic steatosis

Vücut kompozisyon parametreleri ile nonalkolik hepatosteatoz ilişkisi

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ABSTRACT

Objective: Nonalcoholic fatty liver disease (NAFLD) which is strongly correlated with obesity; has been a common worldwide health problem with the improvements in social status. Body composition studies are accepted as a simple follow-up tool for treatment of obesity. Since the correlation of body mass index (BMI) with the hepatosteatosis (HS) is well known; the aim of this study was to assess the usefulness of body composition parameters (BCP) to determine HS on NAFLD patients; using dual bioimpedance analyzer (BIA).

Methods: A total of 253 patients with diagnosis of NAFLD were included into the study. The demographic parameters such as age, sex and BMI were collected; and the ultrasonographic (US) evolution was performed to determine the HS stages. The BCP, such as amount and the percentage of total body fat, fat free mass, and total body water were assessed with the dual bioimpedance analyzer.

Results: There were strong significant correlations between BMI and HS, between BCP and HS ($p<0.05$). However, no statistically significant superiority of BCP was found when compared with BMI regarding diagnostic value for NAFLD ($p>0.05$).

Conclusion: According to our results, it can be concluded that BCP values may have a diagnostic value on diagnosis of NAFLD.

Key words: Body composition, bioimpedance analyzer, nonalcoholic fatty liver disease, obesity

ÖZET

Giriş: Obezite ile sıkı korelasyonu bulunan Nonalkolik yağlı karaciğer hastalığı (NYKH) sosyal statünün iyileşmesi ile birlikte dünya çapında yaygın olarak izlenen bir hastalıktır. Vücut kompozisyonu çalışmaları obezite tedavisi takibinde kullanılmaktadır. Vücut kitle indeksi (VKI) ile hepatosteatozis (HS) arasındaki ilişki iyi bilinmektedir. Çalışmamızda vücut kompozisyon parametrelerinin (VKP) hepatosteatoz teşhisindeki etkinliğinin dual bioimpedans analizör (BIA) kullanılarak araştırılması amaçlanmıştır.

Yöntemler: NYKH tanısı almış 253 hasta çalışmaya dahil edildi. Yaş, cinsiyet, ve VKI gibi demografik parametreler ve ultrasonografik hepatosteatoz verileri kaydedildi. Total yağ kitlesi ve vücut yüzdesi, yağsız vücut kitlesi, total vücut suyu gibi BCP dual bioimpedans analizör ile değerlendirildi.

Bulgular: Hem VKI ve HS, hem de VKP ve HS arasında istatistiksel olarak güçlü korelasyon olduğu izlendi ($p<0,05$). Fakat HS'ın tanısal değeri açısından VKP ve VKI arasında birbirlerine üstünlüğü yoktu ($p>0,05$).

Sonuç: Bulgularımıza göre, NAFLD hastalığında BCP'nin kullanımının tanısal değeri olduğu sonucuna varılabilir.

Anahtar kelimeler: Vücut kompozisyonu, bioimpedans analizör, nonalkolik yağlı karaciğer hastalığı, obezite

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is defined as the accumulation of fat in adipose tissue in the patients with an alcohol use of 30 g/day for men and 20g/day for women; and it is known as the most common hepatic disease [1]. Although the incidence of disease is 2.6% in children, it increases by 5th decade showing a value of 26%; and the most common risk factors are diabetes, obesity and metabolic syndrome [2,3]. It can recent in a

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huge spectrum from simple hepatosteatosis to fibrosis or cirrhosis [4]. It is believed that 10-25% of simple steatosis progresses to NAFLD, and 5-8% of NAFLD progresses to cirrhosis in five years period [5]. Since the clinicopathologic stages of the disease are well known, the etiology and the accepted treatment options have been controversial in the literature. As the incidence of NAFLD is 20-25% of obese population, it is well associated with obesity [6]. Additionally, 80% of patients with a diagnosis of NAFLD show a greater body mass index (BMI) value more than 30 [1]. It shows a significant correlation with obesity, type II diabetes mellitus, metabolic syndrome, chronic renal diseases, colorectal cancer and increased risk for cardiovascular diseases [1]. There is no significant marker in laboratory studies except a slide increase in AST and ALT values [7]. Since the golden standard for diagnosis is biopsy, although the presence of fatty liver in computed tomography (CT) or magnetic resonance imaging (MRI) can help diagnosis, the most common accepted diagnostic tools is ultrasonography (US) with a 89% sensitivity and 77% specifity [8].

Obesity has been a worldwide health problem with the increase of sedentary lifestyle and defined as the excessive fat accumulation in the body with compromising the health of the World Health Organization [9,10]. BMI is a practical evaluation method for obesity with the formula of weight (kg) / (height/m) 2 [9]. As the greater values more than 30 kg/m^2 accepted to classify as obese; individuals with a high percentage of body muscles should not be considered in the definition of obesity. Body composition assessments, including CT, MRI, Dual-energy X-ray absorptiometry (DEXA) and BIA are reliable tools for determination of obesity [11]. But the usefulness of CT, MRI and DEXA with the technical and financial difficulties and disadvantages for accessibility, with the increased radiation explosion; have been discussed in literature before [11,12]. On the other hand bioimpedance analyzer (BIA) is measured by the impedance to an applied small electric current as it passes through the body's water pool [13]. It is accepted as an easy reliable method with its simple application [11,14]. It is pointed that the abdominal obesity has more effective value on risk for cardiovascular diseases and metabolic syndrome [15-17]. The accepted method for determination of abdominal obesity bases on waist circumference measurement, but it seems to be unrealistic. As the most accurate estimation methods are CT or MRI. Yamakage et all suggested BIA to be successful at least than CT [11].

The aim of this study was to assess the usefulness of body composition parameters (BCP) to determine HS on NAFLD patients using dual BIA.

METHODS

Study population

The ethical approval and patients' consent form each patient obtained for the study and the investigation was performed with obeying the principles outlined in the Declaration of Helsinki. Subjects were collected from the patients who were referred to radiology department for the evolution of abdominal US for any reason, in three months period (October-December 2014) prospectively. All patients were questioned for the any presence history of any acute or chronic hepatic disease, history of pregnancy or existing pregnancy and these ones excluded from the study. After careful evaluation a total of 253 patients admitted to the study.

Assessment of hepatosteatosis

Abdominal US was performed with an Aloca Prosound A6 (2009; Hitachi Aloka Medical, Ltd. Tokyo, Japan) equipped with a 7 MHz convex imaging probe. The time gain compensation curve was adjusted in the neutral position and the general gain was calibrated in a way that fluid structures such as the gallbladder contents, inferior vena cava and aorta were presented anechoic. All the sonographic measurements were performed with no pressure on the transducer. Sagittal hepatic sections that encompassed longitudinal images of the right liver lobe and the ipsilateral kidney were obtained. Liver-kidney contrast with two other well-known US findings of fatty liver, vascular blurring and deep attenuation enabled us to grade fatty change semi quantitatively. Fatty infiltration was graded semi-quantitatively into four classes: no steatosis (class 0), mild steatosis (class 1), moderate steatosis (class 2) and severe steatosis (class 3).

Assessment of BIA and BCP

Patients were asked to be ready with 3 hours of fasting, at least 24 hour's period without alcohol and

caffeine intake, without strenuous exercise within 12 hours, and post-micturition for BIA analyses. BIA analyses were obtained with a body composition analyzer TBF-300 (2006,Tanita corp., Tokyo, Japan). The BCP, such as amount and the percentage of total body fat (% Fat) and the amount of fat mass (FM), total body water (TBW), fat free mass (FFM) was recorded. The demographic findings of the subjects were also obtained. BMI was calculated with the formula of weight (kg) / (height-m)^2 and values lower than 19 accepted as weak, values between 19 to 23.99 accepted as normal, values between 24 to 29.99 accepted as overweight, values between 30 to 39.99 accepted as obese and values higher than 40 accepted as morbid obesity.

Statistical analysis

Statistics were run using the STATA 11.0 Software Package (College station, Texas, USA). The results are expressed as mean ± SD, unless indicated otherwise. For the statistical analysis, Student's t test for independent and paired continuous variables and Chi-square test for proportional comparisons of categorical variables were performed. Spearman's test was used for the correlation analyses. Receiver operating characteristic (ROC) curves were used to identify the optimal cut-off points. ROC curves were constructed using 3 cut-off points for the degree of hepatosteatosis measured by the US. To evaluate the performance of measurements sensitivity and specificity of each degree of hepatosteatosis were calculated and the cut-off value producing the best combination of sensitivity and specificity was selected for each measurement. The areas under the ROC curve (AUC) were computed for each measurement and AUC's of fat, fat mass, free fat mass and total body water were compared to BMI AUC. The p-value of <0.05 was considered to be statistically significant.

Table 1. The body composition parameters values according to body mass index (BMI) values

	BMI	Number of patients		Mean		Standard deviation		Minimum		Maximum	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
% fat	Weak	1	2	4.3	8.45		8.84	4.3	2.2	4.3	14.7
	Normal	27	22	14.34	21.08	4.23	4.96	6.1	13.2	22.2	31.5
	Over weight	47	31	24.18	31.06	4.47	5.87	16.1	13.7	41.7	40
	Obese	32	75	30.66	40.29	4.51	5.26	23.3	13	41.6	50.6
	Morbid obese	2	14	32.65	44.44	2.9	2.98	30.6	36.6	34.7	48.7
	Total	**109**	**144**	**23.62**	**35.33**	**7.75**	**9.64**	**4.3**	**2.2**	**41.7**	**50.6**
FM	Weak	1	2	2.4	3.05		3.04	2.4	0.9	2.4	5.2
	Normal	27	22	9.54	11.72	3.54	4.06	3.7	6.2	15.5	21
	Over weight	47	31	19.07	21.99	3.7	5.84	12	9.2	28.3	39.6
	Obese	32	75	28.06	33.17	5.12	6.44	18.4	11.7	39.6	46.5
	Morbid obese	2	14	37.05	45.36	1.91	5.72	35.7	33.5	38.4	52.8
	Total	**109**	**144**	**19.52**	**28.25**	**8.45**	**11.61**	**2.4**	**0.9**	**39.6**	**52.8**
TBW	Weak	1	2	39.8	26.15		6.15	39.8	21.8	39.8	30.5
	Normal	27	22	40.52	31.23	3.98	2.22	34.6	27.5	49.4	36.1
	Over weight	47	31	43.79	35.03	4.47	4.41	29	29.8	52	49.3
	Obese	32	75	46.53	35.79	6.56	4.37	32.6	27.5	60.1	57
	Morbid obese	2	14	56.1	41.33	4.53	3.26	52.9	36.8	59.3	46.9
	Total	**109**	**144**	**43.97**	**35.33**	**5.71**	**4.83**	**29**	**21.8**	**60.1**	**57**
FFM	Weak	1	2	54.3	35.7		8.34	54.3	29.8	54.3	41.6
	Normal	27	22	55.67	42.66	5.77	3.02	47.2	37.6	67.5	49.3
	Over weight	47	31	59.81	47.85	6.1	6.03	39.6	40.7	71	67.4
	Obese	32	75	63.56	48.88	8.96	5.96	44.5	37.6	82.1	77.9
	Morbid obese	2	14	76.6	56.46	6.22	4.46	72.2	50.3	81	64.1
	Total	**109**	**144**	**60.14**	**48.26**	**7.81**	**6.59**	**39.6**	**29.8**	**82.1**	**77.9**

FM: Fat Mass, TBW: Total Body Water, FFM: Fat Free Mass

RESULTS

There was 109 female and 144 male patients with the mean age 48 (range 18-83) years. The range of weight was 35-117.7 kg and the range of height was 143-186 cm. The mean height was 170.3 ± 7.3 cm and 157 ± 6.9 cm, and the mean weight was 79.1 ± 14.1 kg and 75 ± 15.5 kg in men and women respectively. The mean BMI value was 27.43 ± 4.75 in men and was 30.9 ± 6.71 in women. There were 106 patients in class 0, 61 patients in class 1, 78 patients in class 2 and 8 patients in class 3. The incidence of NAFLD was 40.3% in patients with a lower value of 30 and was 78.2% in patients with a higher value of 30 in the means of BMI ($p<0.01$). There was a positive correlation between the BMI value and grade of hepatosteatosis in male and female subjects ($p<0.05$). As the BMI value and grade of hepatosteatosis increases percentage of total body fat, fat mass, total body water and fat free mass increased also ($p<0.05$). These results are shown in Table 1 and 2. In the evolution of %Fat, FM, TBW and FFM compared with BMI; the areas under the ROC curve was statistically significant in each group ($p<0.05$). The results of ROC analyses are shown in Table 3 and figure 1. There was no significant superiority between BCP and BMI in the means of correlation with hepatosteatosis ($p>0.05$). In the analyses of sensitivity and specificity of BMI and BCP considering class 3 HS patients; BMI value at the point of 30 kg/m^2 has 100% sensitivity and 78.2% specificity in men and BMI value at the point of 29 kg/m^2 has 100% sensitivity and 70.6% specificity in women. The percentage of %Fat has 100% sensitivity and 80 % specificity in men at the point of 28.1%, and has 100% sensitivity and 75.5 % specificity in women at the point of 36.2%. The cut-off values of sensitivity and specificity of BMI and BCP are shown in Table 4.

Table 2. The body composition parameters values of patients according to their hepatosteatosis grade

	HS	Number of patients		Mean		Standard deviation		Minimum		Maximum	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
% Fat	0	55	51	21.89	29.99	7.54	10.12	4.3	2.2	36	48.7
	1	21	40	23.81	36.46	9.01	7.36	6.1	16	41.7	50
	2	29	49	25.63	39.19	6.57	8.36	14.7	13	41.6	49.9
	3	4	4	31.88	44.63	3.1	6.15	28.1	36.2	34.7	50.6
	Total	**109**	**144**	**23.61**	**35.33**	**7.75**	**9.64**	**4.3**	**2.2**	**41.7**	**50.6**
FM	0	55	51	17.4	21.38	8.13	10.89	2.4	0.9	35.7	52.8
	1	21	40	18.89	28.63	8.37	7.89	3.7	8.5	39.6	47
	2	29	49	22.29	34.06	7.35	11.11	9.8	5.2	37.5	52.3
	3	4	4	32.05	40.98	6.49	9.74	23.6	27.5	38.4	50.7
	Total	**109**	**144**	**19.52**	**28.25**	**8.45**	**11.61**	**2.4**	**0.9**	**39.6**	**52.8**
TBW	0	55	51	42.8	33.58	5.66	4.17	34.6	27.5	59.4	45.7
	1	21	40	42.77	35.46	5.16	4.1	29	27.5	49.7	49.3
	2	29	49	46.31	36.95	5.45	5.51	37.1	21.8	60.1	57
	3	4	4	49.56	36.63	3.8	4.29	44.1	31.3	52.9	41.4
	Total	**109**	**144**	**43.98**	**35.33**	**5.71**	**4.83**	**29**	**21.8**	**60.1**	**57**
FFM	0	55	51	58.46	45.86	7.73	5.7	47.2	37.6	81.2	62.4
	1	21	40	58.4	48.44	7.06	5.6	39.6	37.6	67.9	67.4
	2	29	49	63.57	50.48	7.33	7.53	50.7	29.8	82.1	77.9
	3	4	4	67.65	50.03	5.18	5.9	60.2	42.7	72.2	56.6
	Total	**109**	**144**	**60.14**	**48.26**	**7.82**	**6.59**	**39.6**	**29.8**	**82.1**	**77.9**

HS: Hepatosteatosis, FM: Fat Mass, TBW: Total Body Water, FFM: Fat Free Mass

Table 3. Areas under the ROC curves of the measures

Man		Class 0	Class 1	Class 2	Class 3
	BMI	0.661*	0.589	0.676	0.925
	% Fat	0.609*	0.530	0.625	0.916
	FM	0.641	0.545	0.672	0.923
	FFM	0.670	0.565	0.720	0.854
	TBW	0.663	0.566	0.706	0.854
Woman					
	BMI	0.770	0.728	0.794	0.892
	% Fat	0.758	0.710	0.784	0.917
	FM	0.774	0.728	0.801	0.912
	FFM	0.695	0.657	0.722	0.730
	TBW	0.695	0.657	0.722	0.733

BMI: Body Mass İndex, HS: Hepatosteatosis, FM: Fat Mass, TBW: Total Body Water, FFM: Fat Free Mass, * P<0,05

DISCUSSION

Obesity has been worlds wide epidemic health problem with the increase in sedentary lifestyle and results with increased incidence of metabolic syndrome, type 2 diabetes mellitus, hypertension and nonalcoholic fatty liver disease. It is estimated that the incidence of NAFLD will be doubled to 2025 [18]. Nguyen et all showed that the incidence of hypertension (HT) increases up to 52.3% in obese patients while it is 18.1% in normal population [19]. Additionally, they showed that the incidences of diabetes mellitus (DM) (2.7→14.2 %), dyslipidemia (8.9→19%) and metabolic syndrome (13.6→39.2%) increased by obesity according to normal population. Some authors suggested that the a resolution and improvement (76.8%, 85.4%) in DM, a 33.20 mg/dl decrement in total cholesterol, 78.5% resolution and 61.7% improvement in HT [20]. Tandra et all showed that there is 60% steatosis, 20-25% NAFLD and 2-3% cirrhosis in obese patients [6]. A study revealed that while the incidence of NAFLD was 9.6% in healthy childhood population, it increases with a percentage of 68.18% in obese children, and pointed that it roles as a predictive factor for coronary heart failure, central obesity and metabolic syndrome [21]. Since all of the diseases can be accepted as multiple variables of a disease when the specific etiological factors excluded.

We found that the incidence of hepatosteatosis was 40.3% in patients with a lower value of the 30 BMI index; it was 78.2% in patients with a higher value 30 BMI index; Bellantani found the incidence of NAFLD was 16.4% in non-obese population while it was 75.8% in obese patients, parallel with our results [22]. Therefore the prevalence of NAFLD is affected by ethnicity, lifestyle and geographical regions [23]. BCP's clinical significant increased with the demonstration of different diseases with obesity. Bioimpedance analyses are the most practical and cheapest method compared with the CT, MR, DEXA, Pet CT in the diagnosis of intra-abdominal visceral obesity [24]. Yamakage et al showed that the bioimpedance analysis has a diagnostic value at least of CT [11]. In our study there was a strong correlation between hepatosteatosis degree and BMI % Fat, FM, TBW and FFM ($p<0.05$) in male and female subjects. Only BMI showed more significant correlation than %fat ($p=0.039$) in men; but there was no statistical significant correlation between other parameters in case of hepatosteatosis evidence.

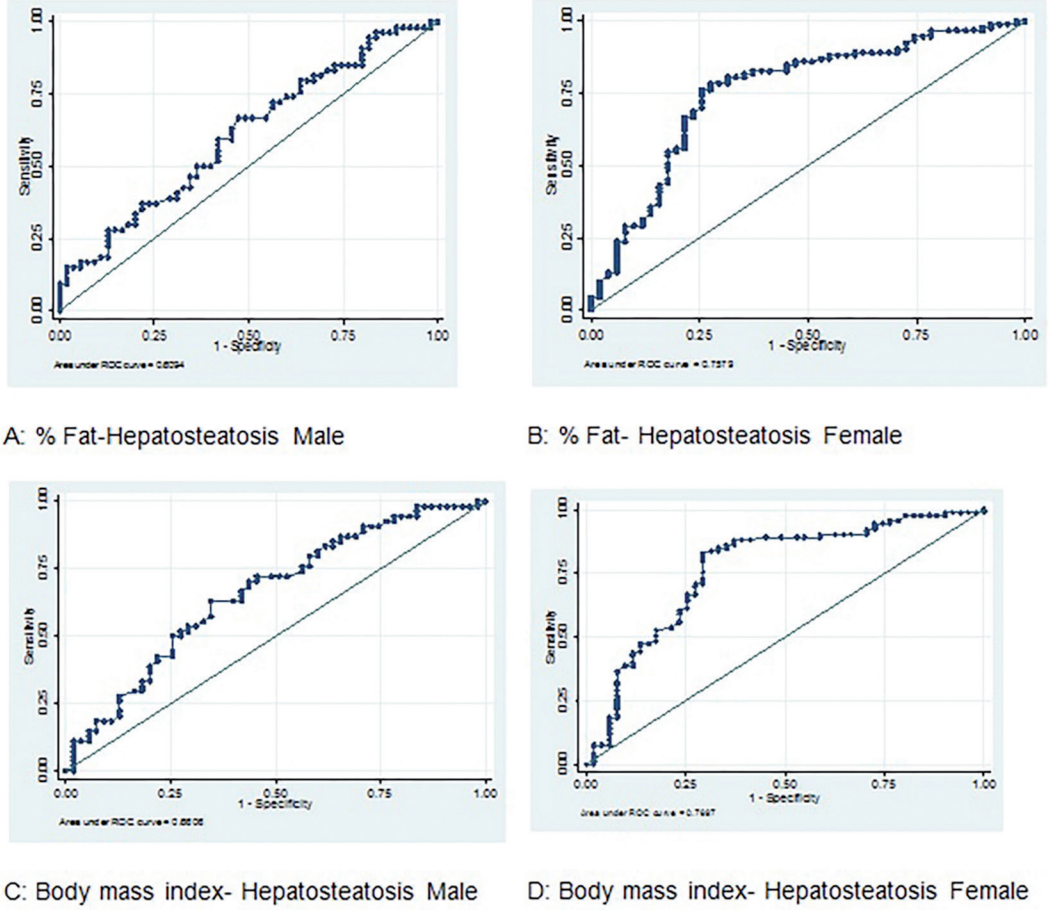
We postulate that BCP values can have a diagnostic value in NAFLD as well as BMI values. Since there is a strong correlation between abdominal adiposity with increased risk for cardiovascular diseases and metabolic syndrome [15-17], but unfortunately we studied the total abdominal obesity but we could not asses the visceral obesity because of the technical insufficiency, and it is the major limitation of our study. Our ongoing workouts will enlighten this issue.

In conclusion as type 2 DM, cardiac failure, hypertension, metabolic syndrome is well associated with obesity, the evidence of these diseases must be assess in obese population; and the BCP can be use for diagnosis of abdominal obesity as well as CT, MRI or DEXA with the superiority of it's some advantages as easy use and an inexpensive modality. There was strong correlation BMI and body composition parameters with NAFLD. When % Fat, FM, TBW, FFM values increases, it should be suspected there is likely to be a NAFLD.

Table 4. The optimal cut-off points for measures and their sensitivities and specifities according to hepatosteatosis class

	Class 1			Class 2			Class 3		
	Cut-off	Sen	Spe	Cut-off	Sen	Spe	Cut-off	Sen	Spe
Man									
BMI	27.9	57.1	65.5	30.1	44.8	80	30	100	78.2
% Fat	28.2	23.8	80	29.8	24.1	87.3	28.1	100	80
FM	23.8	33.3	78.2	24.2	44.8	81.8	23.6	100	78.2
FFM	56.8	71.4	45.6	59	86.2	65.5	60.2	100	65.5
TBW	40.8	85.7	41.8	41.4	86.2	45.6	44.1	100	65.5
Woman									
BMI	27.4	87.5	62.8	29.3	87.8	70.6	29	100	70.6
% Fat	34.3	75	68.6	35.2	83.7	72.6	36.2	100	74.5
FM	25	80	70.6	26.4	83.7	74.5	27.5	100	74.5
FFM	45.1	80	52.9	47.8	67.4	72.6	48.5	75	76.4
TBW	33	80	52.9	31.8	89.8	41.2	31.3	100	35.3

Sen: sensitivity, Spe: specificity, HS: Hepatosteatosis, FM: Fat Mass, TBW: Total Body Water, FFM: Fat Free Mass



A: % Fat-Hepatosteatosis Male

B: % Fat- Hepatosteatosis Female

C: Body mass index- Hepatosteatosis Male

D: Body mass index- Hepatosteatosis Female

Figure 1. Characteristic curves for BMI and body composition parameters

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